Brief General Terminology Abstract: Clinical Protocol for Modification of Tumor Suppressor Gene Expression in Head and Neck Squamous Cell Carcinoma (HNSCC) with an Adenovirus Vector Expressing Wildtype *p53*

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Individuals afflicted with squamous cell carcinoma of the head and neck have a disease process that not only severely affects their quality of life, but also ultimately leads to their death in over 50% of patients. Despite concerted efforts to improve survival with surgery, radiation therapy, and chemotherapy; survival has remained unchanged for over thirty years and approximately 90% of patients that succumb to these cancers do so due to recurrence in the head and neck region. Patients that have failed local/regionally with curative attempts of radiation with or without surgery (for advanced disease) predictably survive a median of six months. However, patients with recurrent head and neck cancer also exhibit readily accessible tumors that can be measured, treated, and biopsied without significant discomfort to the individual. This patient population is the focus of the development of a novel treatment strategy in head and neck cancer.

The general purpose of this study will be to see whether a normal copy of a gene called *p53* can be placed inside the patient's cancer cells and cause the cancer to grow more slowly or to stop growing. We propose to inject a defective virus that contains this *p53* gene that will produce a normal human protein that functions as a tumor suppressor gene. This protein has been shown to cause the death of cancer cells, but not cause cell death of normal cells. The virus, similar to that which produces a common cold, has been altered so it cannot reproduce.

There will be two groups of patients for this study. The first group has advanced recurrent cancer of the head and neck that cannot be surgically removed, whereas in the second group surgery is feasible but will not (in and of itself) cure the patients of their cancer. Patients will receive injections of the defective virus with the normal *p53* gene vector three times weekly for two consecutive weeks. Prior to leaving the hospital, the patient will be checked to make sure that no vector can be identified in any body fluids. A second two week session of therapy, identical to the first, will be undertaken during the second month. For those patients with surgically removable cancers, surgery will be performed three days following their last vector injection. At the time of surgery and prior to the removal of tubes usually placed in surgery, vector with normal *p53* gene will again be put into the surgical site. Those patients with cancers that cannot be removed will continue to receive vector with normal *p53* gene injections three times weekly for two weeks per month unless they should get sick, have a reaction to the injections, tumor continues to grow, or they decide to discontinue treatment.